

Femoral hypoplasia-unusual facies syndrome with bifid hallux, absent tibia, and macrophallus: a report of a Bedouin baby

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Abstract

A male Bedouin baby with the clinical profile of femoral hypoplasia-unusual facies syndrome is described. The phenotype includes bilateral asymmetrical lower limb hypoplasia/aplasia with short remnants of both femora, absent right tibia, bifid right big toe, dysmorphic facies, thoracic/pelvic abnormalities, macrophallus, and bilateral cryptorchidism. This report re-emphasises the previously described rare association of femoral hypoplasia-unusual facies syndrome with preaxial polydactyly and suggests that the clinical spectrum of the syndrome could be stretched further to accommodate other unusual traits, for example, macrophallus and absent tibia.

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Key words: femoral hypoplasia-unusual facies; macrophallus; absent tibia.

Femoral hypoplasia-unusual facies syndrome (FHUFS) (MIM 134780)¹ is characterised by bilateral, mostly asymmetrical, femoral hypoplasia with variable lower limb shortening and non-specific facial dysmorphism. Maternal diabetes mellitus has been found to be associated with a substantial proportion of FHUFS cases, while polydactyly, particularly the preaxial type, represents an unusual trait, documented in only five reported cases of the syndrome.²⁻⁵ Here, we report a case of bilateral asymmetrical lower limb hypoplasia, mainly rhizomelic, with other facial/physical anomalies, large penis, absent right tibia, bifid right big toe, and associated maternal diabetes. The phenotype described in the present report seems to fit in the severe end of the spectrum of FHUFS. The significance of the unusual association with preaxial polydactyly, absent tibia, and macrophallus is discussed.

Case report

We report a malformed male baby delivered in August 1994 at term by LSCS to non-consanguineous Bedouin parents. Apgar scores were 7 and 8 at one and five minutes respectively. The baby's birth weight was 2650 g (between the 3rd and 10th centile), length 46 cm (<3rd centile), and head circumference 34 cm. The parents have two healthy children,

a 4 year old daughter and a 2 year old son, and a history of a stillborn male. The diabetic mother had a 6 year old son and a first trimester spontaneous abortion from a previous marriage.

The malformed baby has facial dysmorphism with a high forehead, prominent eyes, hypertelorism, a small nose, anteverted nostrils, two small haemangiomas over the tip of the nose and on the right upper eye lid, a long philtrum, microstomia, cleft palate, severe micrognathia, and bilateral hypoplastic ears with rudimentary pinnae. Three dimples were noted on the lower left side of the chest wall. The baby had asymmetrical lower limb hypoplasia, with an extremely small right thigh and leg, less hypoplastic left counterparts, and a large, bifid, right big toe. He has macrophallus, hypoplastic scrotum, bilateral cryptorchidism, and left inguinal hernia (fig 1). Skeletal survey at the age of 1 day showed long, hooked clavicles, a small thorax with absent last pair of ribs, bony bridges between the lower ribs, and a cleft close to the anterior cartilagenous end of the right ninth rib. The cervical, thoracic, and lumbar vertebrae appeared normal with mild scoliosis while the last two sacral vertebrae were partially fused and deformed with absent coccygeal ossification. The iliac wings were very narrow with underdeveloped acetabula and unossified pubic rami. The upper extremities showed normal length and ossification, increased distance between the radius and ulna at the elbow joint, and a possible ventral dislocation of the left radius. In the lower extremities, both femora were represented by short remnants with unmineralised epiphyseal ossification centres and the hip joints were not formed. The right leg showed a single bone which seemed to be a bowed fibula. The left leg showed a well formed tibia and an extremely thin and slightly shorter fibula. Each foot showed two tarsal bone ossifications with duplication of the right big toe and overcrowded left metatarsals (fig 2). Ultrasound study showed normal echo patterns of the brain, ventricular system, and abdominal/pelvic internal organs. All laboratory investigations were unremarkable. Cytogenetic studies with banding techniques showed a normal male karyotype (46,XY). Reassessment at the age of 4 months showed that head circumference was 40 cm, length 48 cm, and weight 3510 g, with satisfactory neurodevelopmental progress.

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Figure 1 The baby at the age of 7 days.

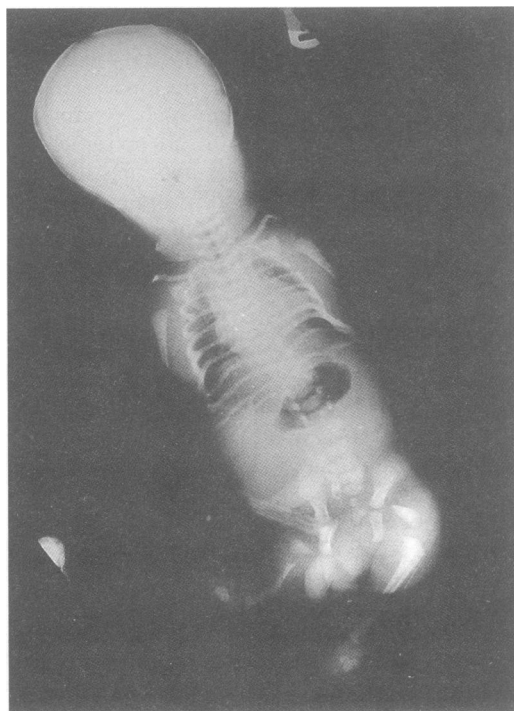


Figure 2 Skeletal survey of the baby at the age of 1 day.

Discussion

Although controversial, the association between maternal diabetes mellitus and congenital malformations in the offspring has been described in numerous reports.^{6,7} Experimental studies have indicated that hyperglycaemia itself is not a major component in producing diabetic embryopathies which are induced instead by some other factors, including genetic disposition and the components of the diabetic state, for example, ketone bodies, somatomedin inhibitors, and low concentrations of insulin.⁸ Isolated congenital anomalies associated with maternal diabetes include macrosomia, microcephaly, anencephaly, spina bifida, holoprosencephaly, ear anomalies, cleft lip/palate, congenital heart disease, neonatal small left colon, malrotation of the bowel, anal/rectal atresia, renal agenesis/multicystic dysplasia, hypospadias, cryptorchidism, and rib/vertebral anomalies.⁶ Preaxial polydactyly of the feet has also been reported as an isolated anomaly in infants of diabetic mothers.⁹ Syndromic embryofetopathies of recognised association with maternal diabetes include caudal regression hypoplasia (BDIS No 914) and FHUFS.

The phenotype described in this report would fit into the severe end of the spectrum of FHUFS. Obvious features of FHUFS clearly shown in the present case include hypoplastic femora, micrognathia, cleft palate, long philtrum, and anteverted nose. The presence of maternal diabetes mellitus adds further support to the diagnosis. Within this framework, the present case specifically bears a striking similarity to the FHUFS profile described by Gleiser *et al*,² Goldberg *et al*,³ Pitt *et al*,⁴ and Baraitser *et al*,⁵ with preaxial polydactyly being the most important shared feature between these cases and the reported Bedouin baby (table).

The present case can be differentiated from the limb/pelvis-hypoplasia/aplasia syndrome (LPHA) (MIM 276820) by the marked asymmetrical lower limb involvement and the different facial dysmorphic features in the reported baby. Both Roberts-SC phocomelia syndrome (MIM 268300) and Robinow syndrome (MIM 180700, 268310) differ from the present case in the symmetrical involvement of the upper and lower limbs, with a mesoacromelic dysplasia in most cases of the two syndromes. The caudal regression syndrome would not be considered in the differential diagnosis since its phenotype does not include important traits described in the present case, for example, facial dysmorphism, cleft palate, ear anomalies, rib fusion, and large penis.

In conclusion, the present report supports the notion that certain unusual traits need to be emphasised as part of the FHUFS profile, for example, polydactyly (particularly hallux duplication) and ear anomalies. Other unusual traits described in the present report, macrophallus and absent tibia, may also emerge as part of the spectrum of the same syndrome.

Important traits of the reported cases of FHUFS and preaxial polydactyly of the foot

	Pitt <i>et al</i> ⁴	Goldberg <i>et al</i> ³	Gleiser <i>et al</i> ²	Baraitser <i>et al</i> ⁵	Present case
Unusual facies	+	+	+	+	+
Cleft palate	+	+	+	+/-	+
Hypoplastic acetabula	?	?	+	+	+
Narrow iliac bone	+	?	+	+	+
Sacral anomalies	?	?	+	+	+
Short femora	+	+	+	+	+
Short/absent tibia	-	-	-	+/-	+
Short/bowed fibula	-	-	-	+	+
Severe talipes	-	-	-	+	-
Preaxial polydactyly of foot	+	+	+	+	+
Radial synostosis	+	-	+	+/-	-
Sprengel anomaly	?	-	+	+/-	-
Ear deformity	+	+	+	+	+
Maternal diabetes	-	-	+	-/+	+

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